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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/871,183	05/31/2001	James N. Higginbotham	P04580US1	9947

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EXAMINER	
GUZO, DAVID	
ART UNIT	**PAPER NUMBER**
1636	9

DATE MAILED: 06/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/871,183	Applicant(s) HIGGINBOTHAM ET AL.	
	Examiner David Guzo	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *37-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 May 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: Attachment on Deposits of Biological Materials.

ATTACHMENT

SUGGESTION FOR DEPOSIT OF BIOLOGICAL MATERIAL

A declaration by applicant or assignee, or a statement by applicant's agent identifying a deposit of biological material and averring the following may be sufficient to overcome an objection or rejection based on a lack of availability of biological material. Such a declaration:

1. Identifies declarant.

2. States that a deposit of the material has been made in a depository affording permanence of the deposit and ready availability thereto by the public if a patent is granted. The depository is to be identified by name and address (See 37 CFR 1.803).

3. States that the deposited material has been accorded a specific (recited) accession number.

4. States that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of the patent (See 37 CFR 1.808(a)(2)).

5. States that the material has been deposited under conditions that assure that access to the material will be available during the pendency of the patent application to one determined by the Commissioner to be entitled thereto under 37 CFR 1.14 and 35 USC 122 (See 37 CFR 1.808(a)(1)).

6. States that the deposited material will be maintained with all the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty (30) years after the date of deposit or for the enforceable life of the patent, whichever period is longer. See 37 CFR 1.806.

7. That he/she declares further that all statements made therein of his/her own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United

States Code and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Alternatively, it may be averred that deposited material has been accepted for deposit under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g., see 961 OG 21, 1977) and that all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

Additionally, the deposit must be referred to in the body of the specification and be identified by deposit (accession) number, name and address of the depository, date of deposit and the complete taxonomic description.

Detailed Action

Applicant's election with traverse of Group I, claims 1-36 in Paper No. 9 is acknowledged. The traversal is on the ground(s) that no separate search is required for an examination of the non-elected group. This is not found persuasive because a search of group I would not be co-extensive with a search of the subject matter of group II. For example, Groups I and II are classified in different classes and subclasses and a search of Group I (compositions and methods for increasing nucleotide transfer and expression in recipient cells) would not involve a search of gene therapy protocols involved in a method of inducing tumor cell regression.

The requirement is still deemed proper and is therefore made FINAL.

Claims 37-42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 9.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 10-15, 20-22 and 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Alemany et al.

Applicants claim a method for increasing nucleotide transfer and expression in recipient cells comprising introducing into the cells a first and second replication incompetent viral vector (one can be a E1 mutant) wherein said first and second viral vectors are complementary in trans so that upon cotransduction viral replication is enabled. The first and/or second viral vectors comprise a nucleotide sequence (expression construct) which can encode a GFP or tumor suppressor gene product or a tumor suicide gene product, the expression of which is desired in the cell and wherein the viral vectors can be adenoviral vectors. Applicants also claim compositions comprising said first and second replication incompetent transcomplementary viral vectors, cells transformed with the vectors and a method of transforming cells using said vectors.

Alemany et al. (cited by applicants, Cancer Gene Therapy, 1999, 6(1), pp. 21-25, see whole article, particularly the Abstract, first two full paragraphs on p. 22 and p. 25) recites a method for nucleotide transfer and expression in recipient cells comprising introducing into the cells (which can be tumor cells) first and second replication incompetent adenoviral vectors (one of which is an E1 mutant in that the E1 coding region is under control of a heterologous promoter sequence) which are complementary in trans so that upon cotransformation viral replication is enabled. Both of the vectors encode and expresses a gene of interest (such as GFP) or can encode and express a tumor suppressor or tumor suicide gene (oncolytic gene(s)). Alemany et al. also recites compositions comprising said vectors, cells transformed with said vectors and a method

for transforming a cell comprising introducing said vectors into the cell. Alemany et al. therefore teaches the claimed invention.

Claims 1-3 and 13 are rejected under 35 U.S.C. 102(b) as being anticipated by Salmons et al.

Applicants claim a method for increasing nucleotide transfer and expression in recipient cells comprising introducing into the cells a first and second replication incompetent retroviral vectors wherein the first and second viral vectors are complementary in trans so that upon cotransfection viral replication is enabled. One of the vectors can comprises a sequence to be expressed, said sequence can be a retroviral sequence. Applicants also claim cells transformed by said vectors.

Salmons et al. Human Gene Therapy, 1993, Vol. 4, pp. 129-141, see whole article, particularly p. 130, second to fourth paragraphs, Fig. 2 and Fig. 3) recites a method for nucleotide sequence transfer and expression in cells comprising introducing into cells a first and a second replication incompetent retroviral vector wherein said vectors are complementary in trans so that upon cotransfection viral replication is enabled. Salmons et al. therefore teaches the claimed invention.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the

applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-5, 6-7, 13-17, 20-21, 23-24, 30-32 and 33-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Perricaudet et al.

Applicants claim a method for increasing nucleotide transfer and expression in recipient cells comprising introducing into the cells a first and second replication incompetent viral (adenoviral) vector (one can be an E1 and/or E3 and/or E4 mutant) wherein said first and second viral vectors are complementary in trans so that upon cotransduction viral replication is enabled. The first and/or second viral vectors comprise a nucleotide sequence (expression construct) which can encode any sequence the expression of which is desired in the cell (it is noted that this includes an adenoviral sequence) and wherein the viral vectors can be adenoviral vectors. Applicants also claim compositions comprising said first and second viral vectors, cells transformed with said vectors and a method of transforming cells using said vectors.

Perricaudet et al. (US 2003/0096787, published 5/22/03, priority to 1994, see whole document, particularly paragraphs 0029, 0034, 0037, 0038, 0055, 0148, 0169, 0175) recites a method for nucleotide transfer and expression in cells comprising introducing into the cells a first and a second replication incompetent adenoviral vector wherein one of the vectors can be a E1 and/or E3 and/or E4 mutant and wherein said vectors are complementary in trans so that upon cotransfection into cells viral replication is enabled. The first and second viral vectors comprise a nucleotide sequence which can encode an adenoviral product (i.e. E4, E3, etc.) the expression of

which is desired in the cell. Perricaudet et al. also recites compositions comprising the viral vectors, cells transformed with the viral vectors and a method of transforming cells with the viral vectors. Perricaudet et al. therefore teaches the claimed invention.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-9, 18-19, 25-26 and 35-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicants claim methods of increasing nucleotide transfer and expression in recipient cells comprising using the recombinant adenovirus 1014 vector and the AVC2.TK vector. Applicants do not recite the generation of these vectors in a manner sufficient to enable the skilled artisan to reliably reproduce the exact claimed vectors. For example, applicants merely recite that "1014 is a mutant with open reading frame 4 expressed." The prior art likewise does not provide the skilled artisan with the wherewithal to reliably reproduce the claimed vectors. Since the claimed vectors are essential for practicing the claimed invention, applicants must deposit these vectors to satisfy the enablement requirements under 35 USC 112, 1st paragraph (See Attachment on Deposits of Biological Materials).

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-9, 11-12, 28-29 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is vague in that applicants recite a vector selected from a group of viruses, not viral vectors. Redrafting the claim to recite a group consisting of retroviral vectors, adenoviral vectors, herpes viral vectors, etc. would be remedial.

Claim 4 is vague in that there is no antecedent basis for the term "said virus" in the claims from which claim 4 depends.

Claim 5 is vague in that there is no antecedent basis for the term "said first or second replication incompetent adenoviral vector".

Claims 11-12 and 28-29 are vague in that they recite a sequence which encodes a tumor suppressor gene or a tumor suicide gene. A nucleotide sequence encodes a protein or polypeptide, not a gene. Redrafting the claims to recite a sequence which encodes a tumor suppressor protein or a tumor suicide gene product would be remedial.

Claim 32 is vague in the recitation of the term "E1-/E3 deletion mutant". It is unclear if applicants are reciting a mutant with a deletion in E1 **and** E3?

No Claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (703) 308-1906. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (703) 305-1998. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Faxes may be sent directly to the examiner at (703) 746-5061.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

David Guzo
June 10, 2003

DAVID GUZO
PRIMARY EXAMINER